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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER
CROUCH, DEBORAH

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,353	STICE ET AL.	
	Examiner	Art Unit	
	Deborah Crouch	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-78* is/are pending in the application.

4a) Of the above claim(s) *36-46 and 78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35 and 47-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election without traverse of group I in Paper No. 5 is acknowledged. Claims 1-35 and 47-77 are examined in this office action.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12, 14, 16-28, 61-68, 70-73 and 75-77 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 5,945,577. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the present species claims is contained within the genus claims of '577. The present claims are directed to methods of cloning a pig by nuclear transfer of a differentiated cell nucleus into an enucleated pig oocyte, followed by activation of the nuclear transfer unit and transfer of the cultured nuclear transfer unit to a host mammal for development into a fetus. Claims 1-24 of '577 are drawn to methods of cloning a nonhuman mammal by nuclear transfer of a proliferating somatic cell nucleus into an enucleated oocyte of the same species as the donor cell, followed by activation of the nuclear transfer unit and transfer of the nuclear transfer unit into a female of the same species as the oocyte so that that the nuclear transfer unit develops into a mammal. Claim 13 specifically states "porcine." Each of the present independent

claims is found in the claims of '577. The presently claimed products are obvious over the methods to produce them as claimed in '577. In particular, '577 states that the cloned mammals are useful as donors in transplantation procedures. Thus, claims 1-24 of '577 anticipate present claims 1-12, 14, 16-28, 61-68, 70-73 and 75-77.

Claims 1-12, 14, 16-28, 61-68, 70-73 and 75-77 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,215,041. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are generic to claims 1-23 of '041. The present claims state that the donor cell is a desired differentiated pig cell or cell nucleus. This language clear covers non-quiescent as claimed in '041 as the present specification defines the donor cells as being proliferating, which is inherently nonquiescent. Claim 8 of '041 specifically states "porcine." In addition, the claimed products would be obvious over the methods claimed in '041 as the specification in '041 states that the methods are useful in the production of the presently claimed products. Thus, claims 1-23 of '041 anticipate present claims 1-12, 14, 16-28, 61-68, 70-73 and 75-77.

Claims 1-28, 61-68, 70-73 and 75-77 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 6,235,969. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046,

29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are generic to claims 1-26 of '969. The present claims state that the donor cell is a desired differentiated pig cell or cell nucleus. This language clearly covers non-quiescent differentiated pig cell as claimed in '969 as the present specification defines the donor cells as being proliferating, which is inherently nonquiescent. In addition, the claimed products would be obvious over the methods claimed in '969 as the specification in '969 states that the methods are useful in the production of the presently claimed products. Thus, claims 1-26 of '969 anticipate present claims 1-28, 61-68, 70-73 and 75-77.

Claims 1-12, 14, 16-35, 61-68, 70-73 and 75-77 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,235,970 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims 29-35 are to methods of producing a cultured ICM cell line using a differentiated pig cells as nuclear donor, and the claims of '970 are to methods of a mammalian cultured inner cell mass cell line using a differentiated somatic mammalian cells as nuclear donor. Both sets of claims require the production of a nuclear transfer unit, activation of the nuclear transfer unit, culturing the nuclear transfer unit to a obtain a pig CICM cell line. The present specification defines the culture of CICM cells as being on fibroblast feeder cells as claimed in '970. Claim 10 of '970 specifically states "pigs." Thus, claims 1-21 of '970 anticipate present claims 29-35. Further claims 19-21 of '970 are to methods of producing a nonhuman mammalian embryo by nuclear transfer, where a proliferating mammalian differentiated cell is the nuclear donor. Claims 1-12, 14, 16-28, 61-68, 70-73 and 75-77 are thus obvious over claims 19-21 of '970 as the method of producing an embryo is inherently part of the present method claims. Claim 20 of '970 specifically states "pigs."

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-35 and 47-77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of cloning a pig comprising inserting a desired differentiated pig cell or cell nucleus into an enucleated pig oocyte to form a nuclear transfer unit, activating the nuclear transfer agent, and transferring multiple nuclear transfer units into the uterus of a female pig and permitting the nuclear transfer unit to develop into a pig, does not reasonably provide enablement for transferring one nuclear transfer unit into the uterus of non-pig recipient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method of cloning a pig comprising inserting a differentiated pig cell or cell nucleus, a differentiated pig cell or cell nucleus wherein a DNA sequence is inserted, removed or modified, a pig CICM cell or cell nucleus, into an enucleated mammalian oocyte, activating the nuclear transfer unit, culturing the activated nuclear transfer unit to greater than the 2-cell stage and transferring the cultured nuclear transfer unit to a host mammal, a method of producing a CICM cell line comprising inserting a differentiated pig cell or cell nucleus, or a differentiated pig cell or cell nucleus wherein a DNA sequence is inserted, removed or modified, into an enucleated mammalian oocyte, activating the nuclear transfer unit, culturing the activated nuclear transfer unit to greater than the 2-cell stage and culturing cells obtained from the nuclear transfer unit, a method of producing a pharmaceutically active protein expressing a transgenic pig offspring, and methods of making chimeric pigs.

At the time of filing, it was well recognized in the art, that in nuclear transfer procedures, female pigs required the development of at least four fetuses to maintain pregnancy (Prather, page 1886, parag. 2, lines 1-4). This is a critical step to the production of either pigs or pig fetuses and must be included in the claims. Further, transferring the NT unit to a non-pig female is not predictable for the production of pigs or pig fetuses. In the production of sheep-goat chimeras, a high incidence of spontaneous abortion was observed, and explained by an incompatibility between the sheep recipient and the goat component

of the conceptus (Fehilly, page 636, col. 2, parag. 2, lines 7-12). The specification provides no guidance for preventing fetal loss when the recipient female is of a non-pig species.

Thus, the skilled artisan would need to engage in an undue amount of experimentation without a predictable degree of success to implement the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,2,5,18,19 29,47,48,50,52,54,55,57,59-65 and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 61 lack antecedent basis for "said cultured NT unit." Further claims 1 and 61 are confusing as a pig fetus is not considered a "pig" by the art. A "pig" is a fully developed, term animal. Applicant should consider breaking the claims into producing a pig embryo, producing a pig fetus, and producing a pig.

Claims 29,47,48,50,52,54,55,57 and 59 are confusing because claim 29 is written as a method of producing an CICM cell line. Claims 47,48,50,52,54,55,57 and 59 read as if they are methods of producing chimeric embryos, fetuses, progeny and offspring. In particular, chimeric fetuses, progeny and offspring do not have the embryonic structure of an inner cell mass. Applicant should re-write claims 47,48,50,52,54,55,57 and 59 as method of producing chimeric embryos, fetuses, progeny and offspring.

Claim 60 is vague as it states "desired differentiated pig CICM cell." All somatic and germ cells would fall into this category. Thus, 61-65 are the same scope as claims 1, 2, 5, 18 and 19.

Therefore, applicant is advised that should claims 1,2,5,18 and 19 be found allowable, claims 61-65 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a

slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19, 20, 27, 28, 65, 66, 68 and 70-75 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cisneros et al (1996) J. Animal Science 74, 925-933.

The claims are drawn to pig offspring and progeny produced by claimed methods of cloning a mammal. However, as claims 19, 20, 27, 28, 65, 66, 68 and 70-75 are product by process claims, a teaching of the same products obtained by a different method serves as anticipatory art against the instantly rejected claims. There is no language in claims 19, 20, 27, 28, 65, 66, 68 and 70-75 which provides any patentable distinction over the pig offspring and progeny in the art.

Cisneros et al teach a commercial pig breed, BCH, and a three breed cross, HYD, (page 926, col. 1, parag. 1, lines 4-6). These pigs inherently are progeny and offspring of parental crosses. Furthermore the claimed pig organs are an inherent feature of the pigs of Cisneros. Without a distinction which indicates a structural or functional difference between the claimed offspring and progeny and those disclosed in Cisneros et al, then Cisneros et al clearly anticipate the claimed invention.

Claims 18,26 and 64 are rejected under 35 U.S.C. 102(b) as being clearly anticipate by Cukrowska et al (1996) Immunology 87, 487-492.

The claims are drawn to pig fetuses produced by claimed methods of cloning a mammal. However, as claims 18,26 and 64 are product by process claims, a teaching of the same products obtained by a different method serves as anticipatory art against the instantly rejected claims. There is

no language in claims 18,26 and 64 which provides any patentable distinction over the pig fetuses in the art.

Cukrowska et al teach Minnesota Miniature pig fetuses (page 488, col. 1, parag. 2, lines 1-3). The pig fetuses of claims 18,26 and 64 are not claimed to have a patentable distinction over the pig fetuses of Cukrowska et al. Therefore, Cukrowska et al clearly anticipate the claimed invention.

Claims 21-23, 67, 76 and 77 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Fodor et al (1994) Proced. Natl. Acad. Sci. 91, 11153-11157.

The claims are drawn to transgenic pig fetuses, offspring and progeny produced by claimed methods of cloning a pig. However, as claims 21-23, 67, 76 and 77 are product by process claims, a teaching of the same products obtained by a different method serves as anticipatory art against the instantly rejected claims.

Fodor et al teach the production of transgenic pigs which express a cDNA sequence encoding human CD59 (page 11155, figure 2). The pigs disclosed by Fodor et al are offspring and progeny of founder pigs (page 11154, col. 1, parag. 2, lines 2-4). As Fodor et al teaches the injection of the transgene into pig embryos, pig fetuses are inherent in the development to term pigs. Claims 21-23, 67, 76 and 77 do not distinguish from transgenic fetuses, offspring, organs or progeny claimed from the fetuses, offspring and progeny taught by Fodor et al. Therefore, Fodor et al anticipate the claimed transgenic fetuses, offspring and progeny.

Claim 31 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Strojek et al 1990) Theriogenology 33, 901-913.

Claim 31 is drawn to a CICM cell line. However, as claim 31 is a product by process claim, a teaching of the same product obtained by a different method serves as anticipatory art against the claim.

Strojek et all teach the culture of ICM cells as cell lines 6-10 (page 903, parag. 5, lines 1-5 and page 907, figure 2). Claim 31 does not distinguish from the ICM cell line taught by Strojek et al. Without

a distinction which indicates a structural or functional difference between the claimed cell line and that disclosed in Strojek et al, Strojek et al clearly anticipates the claimed invention.

Claim 35 is are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Brameld et al (1995) J. Endocrin. 146, 239-245.

Claim 35 is drawn to differentiated pigs cells made by a claimed process. However, as a product by process claim, a teaching of the same product by a different method serves as anticipatory art.

Brameld et al teaches differentiated pig hepatocytes (page 240, col. 1, parag. 2 to col. 2, through parag. 1). Claim 35 does not distinguish from the hepatocytes taught by Brameld et al. Without a distinction which indicates a structural or functional difference between the claimed differentiated cells and those taught by Brameld et al, Brameld et al clearly anticipate the claimed invention.

Claims 49, 51 and 53 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Onishi et al (1994) Biology of Reproduction 51, 1069-1075.

Claims 49, 51 and 53 are drawn to chimeric pig embryos, fetuses, offspring and progeny. However, as product by process claims, a teaching of the same product by a different method serves as anticipatory art.

Onishi et al teach pig chimeras which result from crosses between Chinese pigs and European pigs (page 1071, figure 2). These pigs are chimeric offspring and progeny of the crosses. Pig chimeric embryos and fetuses are an inherent feature to teachings of chimeric pigs. As the claims do not provide a distinction over the chimeric pigs of Onishi et al, Onishi et al clearly anticipates the claimed invention.

Claims 56, 58, 60 and 69 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Rosengard et al (1995) Transplantation 59, 1325-1333.

Claims 56, 58, 60 and 69 are drawn to chimeric pig embryos, fetuses, offspring and progeny, and organs from chimeric pigs, where each has been so that a desired DNA sequence has been inserted, removed or modified. However, as product by process claims, a teaching of the same product by a different method serves as anticipatory art.

Rosengard et al teach pigs, which have had a desired DNA inserted, are germ line mosaics for the DNA sequence encoding human DAF (page 1326, col. 1, parag. 1, lines 4-10). These pigs are deemed to be chimeric as some of the cells of pig contained the transgene and others did not. These mosaic/chimeric pigs are progeny and offspring of the embryo donors. As the mosaic/chimeric pigs are disclosed as beginning as microinjected embryos, transplanted into foster mothers, and allowed to develop to term, the claimed embryos, fetuses and organs are inherent to resultant pig. As the claims do not distinguish over the mosaic/chimeric pigs of Rosengard et al, Rosengard et al clearly anticipates the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Strojek et al (1990) Theriogenology 33, 901-913.

Claim 33 is drawn to a transgenic CICM cell line. However, as claim 33 is a product by process claim, a teaching of the same product obtained by a different method serves as anticipatory art against the claim.

Strojek et all teach the culture of ICM cells as cell lines 6-10 (page 903, parag. 5, lines 1-5 and page 907, figure 2). Strojek et al also teach that ICM cells can be transformed to provide a method for producing transgenic livestock since pronuclear injection of livestock embryos has lead only to limited successes (page 902, lines 5-11). Thus Strojek et al provide the teachings and motivation for the production of ICM cells transformed to comprises a DNA sequence of interest. There is no functional or structural difference between a cell isolated from a transgenic pig or a cell transformed to comprise a DNA sequence of interest in it genome. Thus it would have been obvious to the ordinary artisan at the

time of the instant invention to produce ICM cells that comprised a DNA sequence of interest integrated into its genome. Strojek also teaches that methodology for so transforming totipotent cells was known in the art at the time of filing (page 902, parag. 1, lines 5-8).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (703) 308-1126. The examiner's SPE is Deborah Reynolds, whose telephone number is (703) 305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Art Unit Patent Analyst, Ms. Pauline Farrier, whose telephone number is (703) 305-3550.

The fax number is (703) 308-4242.

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800 1630

Dr. D. Crouch
August 20, 2002